Soluble Factors Secreted by Human Uterine NK Cells Can Inhibit HIV-1 Infection

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Blood NK cells have been shown to play a role in the host immune defense against HIV through direct lysis of HIV infected cells and indirectly through the production of chemokines and cytokines that act on target cells. However, HIV infection usually occurs at mucosal surfaces, and research has shown distinct differences between NK cells in blood and human endothelium. Whether uterine (uNK) cells can help protect against HIV infection is not known. We tested the hypothesis that uNK cells produce soluble factors that can inhibit HIV infection.

uNK clones were treated with or without IL-12 plus IL-15 for 3 days, and conditioned media (CM) from these cultures were tested for their ability to prevent HIV-1_{IIIB} (X4) or HIV-1_{BaL} (R5) infection of TZM-bl cells.

We found that uNK cells showed inhibition against HIV-1_{IIIB} but little against HIV-1_{BaL}. Out of 33 clones tested from 15 individuals, 45% of IL-12/IL-15 stimulated uNK clones showed statistically significant inhibition of TZM-bl cell infection by HIV-1_{IIIB} *(Student's t-test $p<0.05$).* Some uNK clones (24%) inhibited HIV-1_{IIIB} infection without additional cytokine activation. Further, uNK cells whose CM had anti-HIV activity produced significantly higher amounts of SDF-1α than those without anti-HIV-1 activity *($p<0.001$).* However, there was a negative correlation between the production of IFN-γ and anti-HIV activity, as CM from cells that produced > 40pg/ml IFN-γ had no anti-HIV activity *(χ^2 test $p< 0.05$).*

Collectively, these data suggest that cytokine-activated uterine NK cells can release soluble factors with anti-HIV activity, and that this activity correlated with SDF-1α but not with IFN-γ production.

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